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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,562	07/17/2003	Zhizhen Zeng	PF530C1	3320

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EXAMINER	
O HARA, EILEEN B	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/620,562	ZENG ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-21 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-21 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant is advised that claims 1, 9, 11, 16 and 17 are improper Markush claims because the nucleic acids and polypeptides recited there do not serve common functions which are based upon a common property or special technical feature not found in the prior art. The polynucleotides of TR21 and TR22 are distinct and separate inventions because they have different nucleic acid sequences and encode distinct proteins that have different amino acid sequences, structures and functions. Additionally, because the nucleic acids and proteins of TR21 and TR22 are unrelated, antibodies, agonists and antagonists to TR21, and methods of using the polynucleotides, polypeptides, antibodies, agonists and antagonists of TR21, are unrelated to antibodies, agonists and antagonists to TR22, and methods of using the polynucleotides, polypeptides, antibodies, agonists and antagonists of TR22.

A. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-9 and 16, in so far as they are drawn to nucleic acid molecules encoding a TR21 polypeptide or TL 22 polypeptide, classified in class 536, subclass 23.5.

II. Claims 10, 11 and 17, in so far as they are drawn to TR21 and TR22 polypeptides, classified in class 530, subclass 350.

III. Claims 12, 13, 18 and 19, in so far as they are drawn to antibodies to TR21 or TR22, classified in class 530, subclass 388.22, for example.

IV. Claim 14, in so far as it is drawn to a method of treatment by administration of TR21or TR22 protein, classified in class 514, subclass 2.

V. Claims 15 and 20, in so far as they are drawn to a method of inhibiting proliferation of a cell expressing TR21 or TR22 comprising contacting the cell with an antagonistic antibody or antibody fragment or other antagonist of TR21 or TR22 protein, classified in class 424, subclass 198.1, for example.

VI. Claims 15 and 21, in so far they are drawn to a method of enhancing proliferation of a cell expressing TR21 or TR22 comprising contacting the cell with an agonistic antibody or antibody fragment or other agonist of TR21 or TR22 protein, classified in class 424, subclass 143.1, for example.

B. The inventions are distinct, each from each other because of the following reasons:

Inventions I, II and III are independent and distinct, each from each other, because they are products which possess characteristic differences in structure and function and each has an independent utility that is distinct for each invention which cannot be exchanged.

The polynucleotide of **Group I** and the polypeptide of **Groups II** are patentably distinct for the following reasons: polypeptides, which are composed of amino acids, and polynucleotides, which are composed of purine and pyrimidine units, are structurally distinct molecules; any relationship between a polypeptide and polynucleotide is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. Furthermore, searching the inventions of **Groups I and II** together would impose a serious search burden. In the instant case, the search of the polypeptides and the polynucleotides is not coextensive. The inventions of **Groups I and II** have a separate status in the art as shown by their different classifications. In cases such as this one where descriptive sequence information is provided, the sequences are searched in appropriate databases. There is also search burden in the non-patent literature. Prior to the concomitant isolation and expression of the sequence of interest there may be journal articles devoted solely to polypeptides which would not have described the polynucleotide. Similarly, there may have been "classical" genetics papers which had no knowledge of the polypeptide, but

spoke to the gene. Searching, therefore, is not coextensive. Furthermore, a search of the nucleic acid molecules of **Group I** would require an oligonucleotide search, which is not likely to result in relevant art with respect to the polypeptide of **Group II**. As such, it would be burdensome to search the inventions of **Groups I, II and VIII**.

The polypeptide of **Group II** and the antibody of **Group III** are patentably distinct for the following reasons: while the inventions of both **Groups I and III** are polypeptides, in this instance, the polypeptide of **Group II** is a single chain molecule, whereas the polypeptide of **Group III** encompasses antibodies including IgG which comprises 2 heavy and 2 light chains containing constant and variable regions, including framework regions which act as a scaffold for the 6 complementary determining regions (CDRs) that function to bind an epitope. Thus, the polypeptide of **Group II** and the antibody of **Group III** are structurally distinct molecules; any relationship between a polypeptide of **Group II** and an antibody of **Group III** is dependent upon the correlation between the scope of the polypeptides that the antibody binds and the scope of the antibodies that would be generated upon immunization with a polypeptide.

In this case, the polypeptide of **Group II** is a large molecule which contains potentially hundreds of regions to which an antibody must bind, whereas the antibody of **Group III** is defined in terms of its binding specificity to a small structure within **the disclosed SEQ ID NO**. Thus, immunization with the polypeptide of **Group II** would result in the production of antibodies outside the scope of **Group III**. Therefore, the polypeptide and antibody are patentably distinct.

Furthermore, searching the inventions of **Group II** and **Group III** would impose a serious search burden. The inventions have a separate status in the art as shown by their different classifications. A polypeptide and antibody which to the polypeptide require different searches. An amino acid search of the full-length protein is necessary for a determination of novelty and unobviousness of the protein. However, such a search is not required to identify the antibodies of **Group III**. Furthermore, antibodies which bind to an epitope of a polypeptide of **Group II** may be known even if a polypeptide of **Group II** is novel. In addition, the technical literature search for the polypeptide of **Group II** and the antibody of **Group III** is not coextensive, e.g. antibodies may be characterized in the technical literature prior to discovery of, or sequencing of, their binding target.

The polynucleotide of **Group I** and the antibody of **Group III** are patentably distinct for the following reasons: the antibody of **Group III** includes, for example, IgG which comprises 2 heavy and 2 light chains containing constant and variable regions, including framework regions which act as a scaffold for the 6 complementary determining regions (CDRs). Polypeptides, such as the antibody of **Group III** which are composed of amino acids, and polynucleotides, which are composed of nucleic acids, are structurally distinct molecules. Any relationship between a polynucleotide and polypeptide is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. In the present claims, a polynucleotide of **Group I** will not encode an antibody of **Group III**, and an antibody of **Group III** cannot be encoded by a polynucleotide of **Group I**. Therefore, the antibody and polynucleotide are patentably distinct.

The antibody and polynucleotide inventions have a separate status in the art as shown by their different classifications. Furthermore, searching the inventions of **Groups I** and **III** would impose a serious search burden since a search of the polynucleotide of **Group I** would not be used to determine the patentability of an antibody of **Group III** and vice-versa.

Invention I and each of inventions IV-VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the nucleic acids of invention I are not used in the methods of treatment of inventions IV-VI.

Inventions II and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptides can be used in a method of making antibodies, which is a materially different method from the method of treatment.

Invention II is unrelated to each of inventions V and VI. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the polypeptide is not used in the methods of treatment with antibodies.

Invention III is related to each of inventions V and VI as product and process of use. In the instant case the antibodies can be used in a method of purifying polypeptides, which is a materially different method from the method of treatment.

Inventions III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the antibodies are not used in the methods of treatment with polypeptides.

Inventions V and VI are unrelated. The method of inhibiting cell proliferation with an antagonist antibody of invention VI is patently distinct from the method of enhancing cell proliferation with an agonist antibody of invention VII. They are drawn to treatment with different compounds which have opposite effects, and are therefore patently distinct.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification and/or different search requirements, and the search required for each group is not required for the other groups because each group requires a different non-patent literature search due to each group comprising different products and/or method steps, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

C. *Further Restriction Within Groups I-VI*

For whatever group is elected, further restriction within the elected group is required, as follows.

Group I

If Group I is elected, Applicants must further elect ***one*** nucleic acid, SEQ ID NO: 1 and encoding TR21 polypeptide, or SEQ ID NO: 3 and encoding TR22 polypeptide.

Groups II, IV

If Group II or IV is elected, Applicants must further elect either TR21 or TR22 polypeptide.

Group III, V, VI

If Group III, V or VI is elected, Applicants must further elect antibody to either TR21 or TR22 polypeptide.

Although classifications for the nucleic acids, proteins, antibodies and methods of treatment are overlapping, for instance 536/23.1, each represents a patentably distinct product, having different chromosomal locations and sequences for the nucleic acids of group I, different amino acid sequences, structures and activities for the polypeptides of group II, and different amino acid sequences and binding specificities for the antibodies of group III, and each would require separate sequence searches. Therefore the methods using the proteins and antibodies are also patentably distinct. Furthermore, searching the different inventions of each of the groups would impose a serious search burden since a search of one of the polynucleotides of group I, for example, would not be used to determine the patentability of the other polynucleotides, and vice-versa.

Applicants are advised that this is not a species election.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Rejoinder Under Ochiai/Brouwer

The examiner has required restriction between product and process claims. Where Applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04.

Process claims that depend from **or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or notice of allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully

examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (571) 272-0829.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://portal.uspto.gov/external/portal/pair. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Eileen B. O'Hara, Ph.D.

Patent Examiner

EILEEN B. O'HARA
PATENT EXAMINER